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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,946	10/04/2005	Akiko Itai	P27674	5544

7055 GREENBLUM & BERNSTEIN, P.L.C. 1950 ROLAND CLARKE PLACE RESTON, VA 20191	7590 06/20/2007
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EXAMINER	
HAVLIN, ROBERT H	

ART UNIT	PAPER NUMBER
1609	

NOTIFICATION DATE	DELIVERY MODE
06/20/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

gbpatent@gbpatent.com
pto@gbpatent.com

Office Action Summary

Application No.

10/529,946

Applicant(s)

ITAI ET AL.

Examiner

Robert Havlin

Art Unit

1609

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 April 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8, 12-14 and 21-30 is/are pending in the application.
- 4a) Of the above claim(s) 1-8, 14 and 21-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 12, 13 and 27-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 10/4/05.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____.

DETAILED ACTION

Status of the claims: All of the claims were initially drawn to products when filed.

Claims 3-11 were amended on filing, claims 14-20 were newly presented at filing.

Along with the response to the requirement for restriction, the claims were further amended to cause claims 1-8, 14, to read on methods (previously reading on a product); claims 9-11 and 15-20 were cancelled; claim 12 was amended to better fit within the requirement for restriction; claims 21-26 are newly presented method claims; claims 28-30 are newly presented product claims.

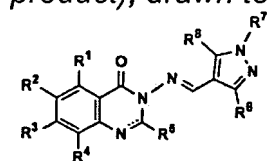
Priority: This application is a 371 of PCT/JP03/12648 (10/02/2003) claiming priority to JAPAN 2002-291114 (10/03/2002).

IDS: The IDS filed on 10/04/2005 has been considered.

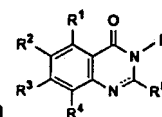
Election/Restrictions

- Applicant's election with traverse of Group I:

Group I, original claims 1-20 (not all claims as amended are directed to the product), drawn to a product of the formula:



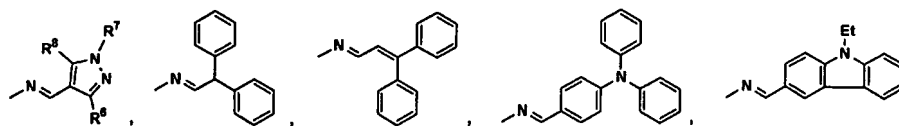
, wherein the dashed line represents either a single or double bond.



broadened by the examiner to include compounds of the formula

wherein R is one of the following:

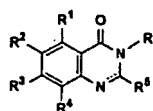
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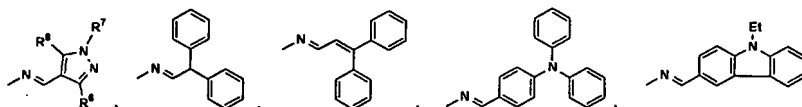
in the reply filed on

4/5/2007 is acknowledged. The traversal is on the ground(s) that the reference cited (Gao, US 6,429,311) does not anticipate the pending claims following amendments.

This is not found persuasive because the currently pending claims are drawn to a genus



, wherein R is one of the following:



which leads to a technical

feature as previously cited to be taught by Gao, furthermore the references cited below in the 103 rejection evidence the lack of a special technical feature in the claims.

Therefore this application lacks unity of invention (please see 37 CFR 1.475).

The requirement is still deemed proper and is therefore made FINAL.

In accordance with the requirement for restriction, claims 1-8, 14, 21-26 drawn to processes of using products of Group I are hereby withdrawn from consideration in this action. Subject matter falling within Group I, currently pending claims 12, 13, and 27-30 are under examination in this action.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

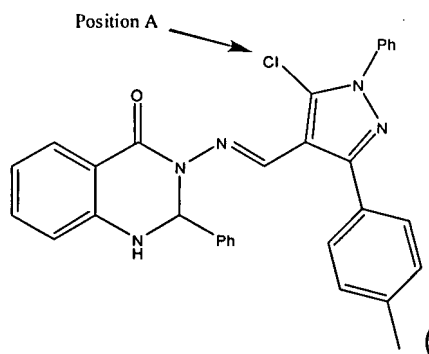
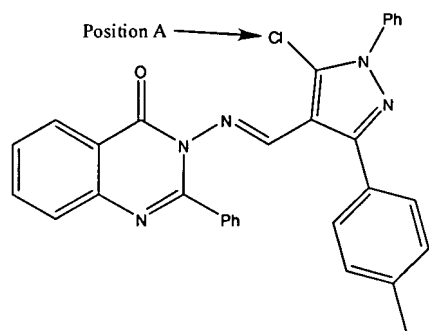
(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

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invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

3. Claims 12, 13, 27-30 rejected under 35 U.S.C. 103(a) as being unpatentable over Farghaly et al. (Alexandria J. of Pharm. Sci., 1990, vol 4, p. 52-6) in view of Hadjipavlou-Litina (Curr. Med. Chem., 2000, v. 7, p. 375-388), Bonola et al. (J. Med. Chem., 1970, v. 13, p. 329-332), Kirchner et al. (US 3,843,654), and Kurup et al. (Chem. Rev., 2001, v. 101, p. 2727-2750).

The claims read on a genus of compounds including the species of

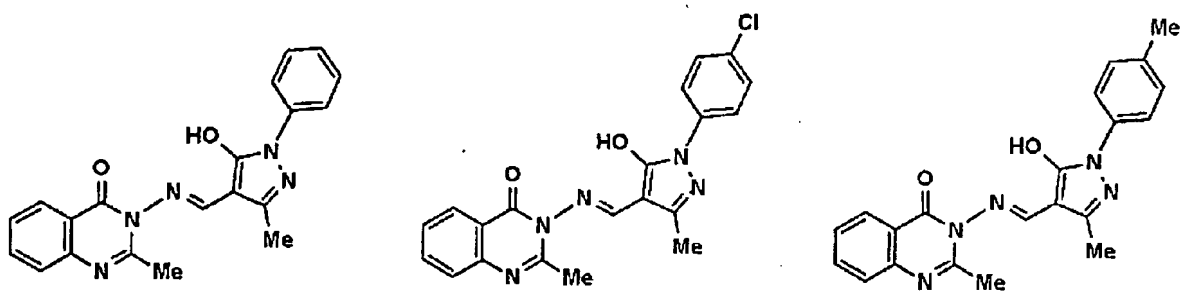


at position A (as annotated above) can be halogen, hydroxyl, or C₁-C₆-alkoxy which

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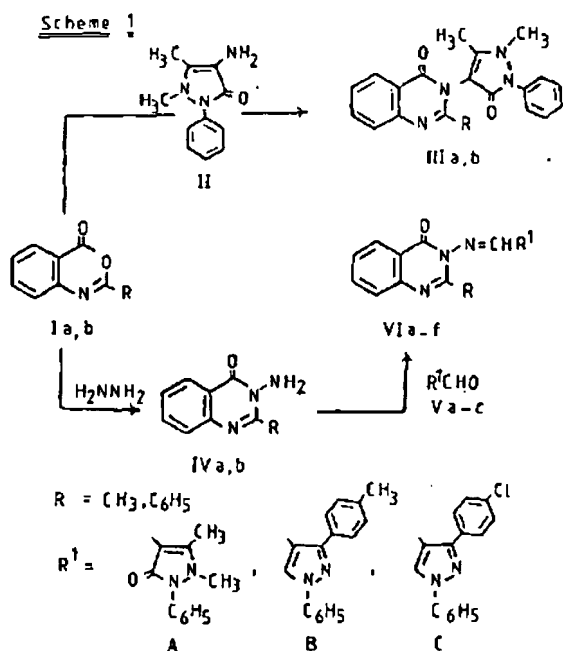
may be substituted. Claim 12 provides that compounds of group β below are excluded:

[Compound group β]



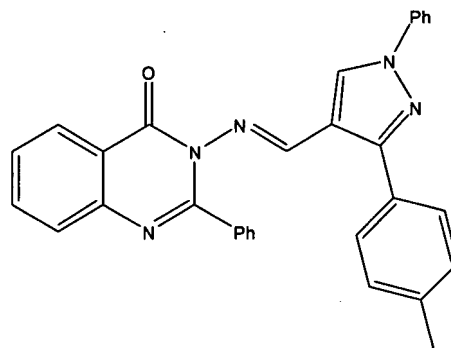
Determination of the scope and content of the prior art

Farghaly et al. teaches the synthesis and screening for anti-inflammatory biological activity of a genus of compounds including those made in scheme 1:



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Specifically, compounds of formula VI wherein R (as defined in scheme 1) is C₆H₅ and



R1 is 'B' to give a compound of the formula:

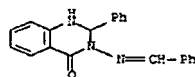
Furthermore, the reference teaches the desirability of compounds of formula VIa for anti-inflammatory activity relative to other compounds (p. 53, col. 2).

Hadjipavlou-Litina teaches the use of quantitative structure-activity relationship QSAR in optimizing the potency of compounds for use as anti-inflammatory drugs (see abstract). Specifically, the reference also teaches the anti-inflammatory activity of the class of compounds called quinazolinones (same as the instant invention) and hiw derivatives were found to be effective inhibitors of prostaglandin synthetase.

From page 379: Non-acidic Anti-inflammatory Agents

*Compared with aryl-acids, the pharmacological profile of the non-acidic compounds is more structure dependent and they generally produce less gastrointestinal irritation. Even with the absence of the carboxyl group, some are potent PGs inhibitors. The non-acidic agents may be categorized as substituted triaryls, **quinazolinones** and a miscellaneous group with different biochemical properties. Several combinations of three aryl groups, such as **two phenyl and a five membered heterocycle, in a fused or angular stereochemical configuration** (e.g. **substituted indolylderivatives and substituted phenyl-oxazolopyridines**) have been found to exert anti-inflammatory activity. Among various analogues **proquazone and ciproquazone** were found to be effective and to act as reversible inhibitor of prostaglandin synthetase. Diftalone was also found to be a non-acidic moderately active anti-inflammatory compound. Etodolac and nabumetone are new compounds, inhibitors of COX, possessing anti-inflammatory activity.*

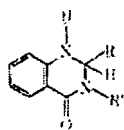
Kirchner et al. teaches a genus of quinazolinones and the specific member of



on col. 3, line 55 and their use as pharmaceuticals.

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Bonola et al. teaches a genus of compounds having the core formula:

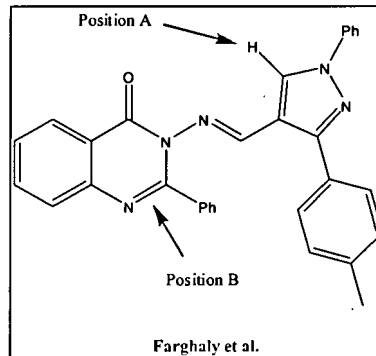
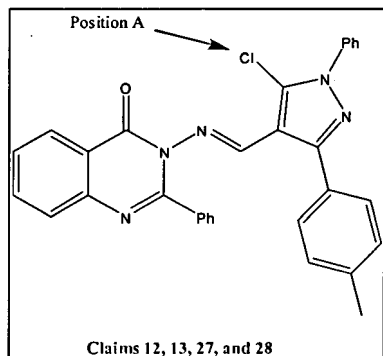


with pharmacological activity including antipyretic (anti-inflammatory) effects.

Kurup et al. teaches the QSAR method on receptor antagonists including quinazolinones, specifically modifying substitutions on rings with hydroxyl, alkoxy, and halogens to determine a quantitative numerical formula assisting in arriving at the optimally active pharmaceutical. Tables 8 and 11 for example are for compounds VIII and XI and explore substitutions such as halogens. Furthermore, numerous other compounds with pyrazoles are explored with substitutions including halogens such as XXVI, XXXI, XXXII, XXXIV, XXXVI, etc.

Differences between the prior art and the claims

The difference between the instant claims 12, 13, 27, and 28 and the teachings of Farghaly et al. is the substitution of a chlorine atom (or any halogen, hydroxyl, or alkoxy) at position A as annotated below:



The difference between the instant claims 29 and 30 and the teachings of Farghaly et al. is the bond at position B (as annotated above) is a single bond instead of a double bond in addition to the substitution described above at position A. **Kirchner et**

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al. teaches the single bond at position B, however in place of the substituted pyrazole ring there is a phenyl group.

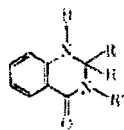
Finding of prima facie obviousness – rationale and motivation

One of ordinary skill in the art pursuing the compounds as anti-inflammatory pharmaceuticals (or any of the other activities described in the specification) would reasonably be expected to be aware of the teachings of Farghaly et al. since the title of the article is "Non-steroidal anti-inflammatory agents. III: synthesis of pyrazole derivatives of 4(3H)-quinazolinones" which is clearly the identical field of endeavor as the instant application. Furthermore, Farghaly et al. specifically points out that the compounds with the formula VI (same as the one annotated above) had improved effects for anti-inflammatory activity relative to other configurations of compounds (col 2, p 53).

Taking the compound taught by Farghaly et al. and modifying it by substituting a chlorine atom at position A would have been obvious to one of ordinary skill in the art in view of the teachings of Hadjipavlou-Litina and Kurup et al. One of ordinary skill in the art of pharmaceutical development would be well aware of the QSAR methods taught by Hadjipavlou-Litina and Kurup et al. due to their being in the same field. QSAR is a methodology which directs the person of ordinary skill in the art to make prescribed substitutions on rings at positions suspected to be important in the activity of a pharmaceutical in order to arrive at the optimally effective pharmaceutical. As described above, the Kurup et al. teaches halogen substitutions on pyrazole rings just as required to arrive at the instantly claimed invention.

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Bonola et al. teaches a group of compounds with anti-inflammatory activity with the core structure identical to the compound described in instant claims 29 and 30 of



thereby suggesting to one of ordinary skill in the art that modifying the bond at position B in the Farghaly et al. compound to a single bond would be desirable for a pharmaceutical compound with anti-inflammatory activity. Furthermore, Kirchner et al. teaches a genus of compounds as pharmaceuticals with a more similar core to the instant invention thus providing one of ordinary skill in the art with additional motivation to modify the bond at position B to arrive at the instant invention.

Since the references used in arriving at the instant invention are all in the related art of pharmaceuticals and even anti-inflammatory pharmaceuticals, there would be a reasonable expectation of success for the person having ordinary skill in the art to arrive at the claimed invention. Therefore the claims are obvious over the prior art.

Conclusion

All claims are rejected.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Havlin whose telephone number is (571) 272-9066. The examiner can normally be reached on Mon. - Fri., 7:30am-5pm EST.

If attempts to reach the examiner by telephone are unsuccessful the examiner's supervisor, Cecilia Tsang can be reached at (571)-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Robert Havlin
Examiner

/RH/


CECILIA TSANG
SUPERVISORY PATENT EXAMINER